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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,987	09/19/2005	Jianming Chen	133697-0006	8330

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BUTZEL LONG
350 SOUTH MAIN STREET
SUITE 300
ANN ARBOR, MI 48104

EXAMINER	
SCHUBERG, LAURA J	
ART UNIT	**PAPER NUMBER**
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,987	CHEN ET AL.	
	Examiner	Art Unit	
	Laura Schuberg	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18 is/are rejected.

7)☒ Claim(s) 6 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/19/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending and have been examined on the merits.

Priority

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in China on 03/20/2003. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet.

If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of

such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

The information disclosure statement filed 09/19/2005 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claim 6 is objected to because of the following informalities: The term "prepare" in line 3 should be "preparing". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the liposome structures" in line 2. There is insufficient antecedent basis for this limitation in the claim.

For examination purposes the "the liposome structures" are interpreted to be "preliposomal structures".

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8, 10, 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004).

Claim 1 is drawn to CoQ10- containing preliposomes, which contain spongiamine in the liposome structures.

Dependent claims include wherein the preliposomes are a granular, lyophilized solid; concentrations of CoQ10; additional lipid components and formulation as a pharmaceutical.

Claim 6 is drawn to a method of preparing the CoQ10-containing preliposomes of claim 1 which comprises: preparing a lipid solution by one of a) melting CoQ10 and spongiamine; and b) dissolving CoQ10 and spongiamine in an organic solvent; and applying the lipid solution to an underlay to produce the CoQ10-containing preliposomes which contain spongiamine.

Dependent claims include the composition of the underlay; wherein the lipid solution is applied to the underlay by one of several methods; wherein the resulting mixture is subject to at least one of several drying methods and the composition of the underlay.

Yatvin teaches pharmaceutical compositions and methods of making wherein the proliposomal compositions include an antioxidant (page 4 para 59), a ceramide and cholesterol (page 4 para 58). Wherein the composition is in dry granular form (page 4 para 55) lyophilized and then compressed into a solid tablet is taught (page 5 para 73).

The presence of the cholesterol lowers the melting point of the lipid solution so that a lower temperature may be used to melt the antioxidant and lipid (ceramide) (page 6 para 80). The use of lactose in the method is taught as well as dissolving the components with an organic solvent (page 4 para 62 and page 5 para 70-71).

Yatvin does not specifically teach including coenzyme Q10 as the antioxidant or spongiamine as the ceramide.

Keller teaches a method of making a preliposome formulation and then dehydrating it. Biologically active materials for the preliposomal formulation include nutritional supplements and antioxidants such as coenzyme Q10 (page 4 claim 5). The concentration of CoQ10 is indicated in example 2 as 1.29 % (page 3). Ceramides and sphingolipids are taught as suitable as the lipid component (page 2 para 16). Cholesterol is taught as added to the preliposome formulation (page 2 para 16). Liposomal formulations with ceramides are taught to increase bioavailability of an antioxidant which is poorly absorbed orally (page 1 para 10-page 2).

Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation). Ceramides are taught to be the main structure for forming sphingolipids and offer advanced activity in anti-tumor, anti-virus, anti-hepatotoxic and immunization uses as well as highly effective for moisturizing (page 2 of translation). The data show that spongiamine are characterized by the classical structure of ceramides (page 4 of translation).

Applicant's disclosure teaches that methods such as a membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay are known in the prior art (page 4 lines 11-14).

Therefore, one of ordinary skill in the art would have been motivated to include CoQ10 in the method and composition of Yatvin as the antioxidant because Keller teaches that CoQ10 is a suitable antioxidant to be used in a preliposomal formulation. One of ordinary skill in the art would have had a reasonable expectation of success because Yatvin teaches that proliposomes are ideally suited for lipophilic compounds and have implications for developing formulations that stabilize encapsulated drugs (page 8 para 97). The concentration of CoQ10 taught by Keller of 1.29% falls in the same ranges as claimed by Applicant.

One of ordinary skill in the art would have been motivated to include the ceramide spongiamine in the method of Yatvin because Wen-Jian Lan et al. teach the discovery of two new ceramides named Spongiamine A and Spongiamine B that were isolated from the sponge *Spongia* sp. (abstract and page 3 of translation) and have numerous benefits (page 2 of translation). One of ordinary skill in the art would have had a reasonable expectation of success because Wen-Jian Lan et al. teach that spongiamine are characterized by the classical structure of ceramides (page 4 of translation); are the main structure for forming sphingolipids; and Keller teaches that sphingolipids as well as ceramides are also suitable as the lipid component of a preliposome (page 2 para 16).

One of ordinary skill in the art would have been motivated with a reasonable expectation of success of using the methods of membrane dispersion method or a melt method or an infuse method to obtain CoQ10-containing liposomes which contain the underlay since they are known methods in the prior art as disclosed by Applicant.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Therefore, the combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious Applicant's invention as claimed.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) as applied to claims 1-8, 10 and 12-18 above, and further in view of Hoppe et al. (US 6,261,575).

Claim 9 includes formulating the composition of claim 1 as a cosmetic.

The combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious claim 1 as described above, but do not mention formulating the composition as a cosmetic.

Hoppe et al. teach a cosmetic formulation of a composition that contains 0.05-1 % CoQ10 and cholesterol (column 4, lines 35-45). The reference also teaches that it is

advantageous to add ceramides to the formulations (column 5 lines 45-48) and that they can be encapsulated in liposomes with ceramides as well (column 6 lines 24-28).

Therefore, one of ordinary skill in the art would have been motivated to incorporate the preliposomal formulations of Yatvin containing CoQ10 and ceramides into cosmetic formulations because Hoppe et al. teach that these ingredients are advantageous for cosmetic skin care products. One of ordinary skill in the art would have been motivated to add spongiamine as the ceramide because Wen-Jian Lan et al. teach that ceramides such as spongiamine offer advanced activity in anti-tumor, anti-virus, anti-hepatotoxic and immunization uses as well as highly effective for moisturizing (page 2 of translation). One of ordinary skill in the art would have had a reasonable expectation of success because Keller teaches that compositions containing CoQ10 in liposomal format can be administered topically as well as orally (page 2 para 15).

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., and Hoppe et al. render obvious Applicant's invention as claimed.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yatvin (US 6,824,790) in view of Keller (US 2002/0039595) and Wen-Jian Lan, et al. (Acta Scientarium Naturalium Universitatis Sunyatseni ,Jan. 2004) as applied to claims 1-8, 10 and 12-18 above, and further in view of Chen et al. (Journal of Pharmaceutical Sciences, 1987) and Weithmann et al. (US 5,318,987).

Claim 11 is drawn to the method of claim 6 wherein the lipid solution is applied to the underlay using a fluidized bed and the organic solvent is evaporated in the fluidized bed.

The combined teachings of Yatvin, Keller, and Wen-Jian Lan, et al. render obvious claim 6 as described above, but do not specifically mention using a fluidized bed.

Chen et al. teach that use of a fluidized bed is advantagous for formulating proliposomes because 1) the film coating technology using the fluidized bed is well established and processable; 2) various cores and coating materials are available or easy to prepare; and 3) it is cost effective to prepare liposomes for drug delivery by oral and/or many other routes of administration (page 1, last paragraph).

Weissman et al. teach a method of preparing antioxidant/lipid solutions in a liposomal formulation using a fluidized bed to form tablets that contain carriers such as various sugars (lactose) (column 11-column 12). Weissman et al. also teach that better results are obtained if the lipophilic antioxidants are additionally incorporated during the preparation of liposomes as components thereof (column 51 lines 44-46). These formulations can be used in pharmaceuticals as well as cosmetics (column 9 lines 34-40).

Therefore, one of ordinary skill in the art would have been motivated to use the fluidized bed technology in the method of Yatvin to form the preliposomal composition because of the advantageous taught by Chen et al. above. One of ordinary skill in the art would have had a reasonable expectation of success because Weissman et al.

teach that fluidized bed technology has been successfully used to form liposomal formulations with lipophilic antioxidants and CoQ10 is a lipophilic antioxidant.

Therefore, the combined teachings of Yatvin, Keller, Wen-Jian Lan, et al., Chen et al. and Weithmann et al. render obvious Applicant's invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651

Laura Schuberg